

We claim:

- 1 1. A method of determining the presence of an inflammatory disease in a patient, the
2 method comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample from the
4 patient; and
- 5 (b) comparing said amount of OP-1 protein with a predetermined standard;
6 wherein a difference in the amount of OP-1 protein present in said sample and the predetermined
7 standard is indicative of the presence of inflammatory disease.
- 2 2. A method of determining the presence of an inflammatory disease in a patient, the
method comprising the steps of
- 3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample from the
patient; and
- 4 (b) comparing said amount of OP-1 mRNA with a predetermined standard;
5 wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined
6 standard is indicative of the presence of inflammatory disease.
- 1 3. A method for determining the clinical severity of an inflammatory disease in a patient,
2 the method comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample; and
- 4 (b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 protein present in joint tissue samples
6 obtained from members of a population having said inflammatory disease with the
7 clinical severity of said disease,
8 thereby to determine the clinical severity of the inflammatory disease in said patient.

1 4. A method for determining the clinical severity of an inflammatory disease in a patient,
2 the method comprising the steps of

- 3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample; and
4 (b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 mRNA present in joint tissue
6 samples obtained from members of a population having said inflammatory disease with
7 the clinical severity of said disease,

8 thereby to determine the clinical severity of the inflammatory disease in said patient.

1 5. The method of any one of claims 1-4, wherein the joint tissue sample comprises a tissue
2 selected from the group consisting of cartilage, ligament, meniscus, tendon, synovium, synovial
3 fluid and intervertebral disc tissue.

1 6. The method of any one of claims 1-4, wherein the joint tissue sample comprises synovial
2 fluid.

1 7. The method of claim 1 or 3, wherein the step of determining an amount of OP-1 protein
2 present in the joint tissue sample comprises performing an enzyme-linked immunosorbent assay
3 (ELISA).

1 8. The method of any one of claims 1-4, wherein the inflammatory disease is selected from
2 the group consisting of rheumatoid arthritis, lupus erythematosus, gout, fibromyalgia syndrome,
3 polymyalgia rheumatica, psoriasis, bacterial infection, viral infection and fungal infection.

1 9. A method of determining the presence of an age-related tissue disorder in a patient, the
2 method comprising the steps of;

- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample from the
4 patient; and
5 (b) comparing said amount of OP-1 protein with a predetermined standard,

6 wherein a difference in the amount of OP-1 protein present in said sample and the predetermined
7 standard is indicative of an age-related tissue disorder.

1 10. A method of determining the presence of an age-related tissue disorder in a patient, the
2 method comprising the steps of;

3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample from the
4 patient; and

5 (b) comparing said amount of OP-1 mRNA with a predetermined standard,

6 wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined
7 standard is indicative of an age-related tissue disorder.

11. A method of determining the presence of a disorder characterized by accelerated or
abnormal tissue aging in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 protein present in a joint tissue sample from the
patient; and

(b) comparing said amount of OP-1 protein with a predetermined standard,

wherein a difference in the amount of OP-1 protein present in said sample and the predetermined
7 standard is indicative of a disorder characterized by accelerated or abnormal tissue aging.

12. A method of determining the presence of a disorder characterized by accelerated or
abnormal tissue aging in a patient, the method comprising the steps of;

(a) determining an amount of OP-1 mRNA present in a joint tissue sample from the
patient; and

(b) comparing said amount of OP-1 mRNA with a predetermined standard;

6 wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined
7 standard is indicative of a disorder characterized by accelerated or abnormal tissue aging.

- 1 13. A method for determining the clinical severity of an age-related tissue disorder in a
2 patient, the method comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample; and
- 4 b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 protein present in joint tissue samples
6 obtained from members of a population having said age-related tissue disorder with the
7 clinical severity of said disorder,
- 8 thereby to determine the clinical severity of the age-related tissue disorder in said patient.
- 1 14. A method for determining the clinical severity of an age-related tissue disorder in a
2 patient, the method comprising the steps of
- 3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample; and
- 4 b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 mRNA present in joint tissue samples
6 obtained from members of a population having said age-related tissue disorder
7 with the clinical severity of said disorder,
- 8 thereby to determine the clinical severity of the age-related tissue disorder in said patient.
- 1 15. A method for determining the clinical severity of a disorder characterized by accelerated
2 or abnormal tissue aging in a patient, the method comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample; and
- 4 b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 protein present in joint tissue samples
6 obtained from members of a population having said disorder with the clinical severity of
7 said disorder,

8 thereby to determine the clinical severity of the disorder characterized by accelerated or
9 abnormal tissue aging in said patient.

1 16. A method for determining the clinical severity of a disorder characterized by abnormal
2 tissue aging in a patient, the method comprising the steps of

3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

4 b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 mRNA present in joint tissue
6 samples obtained from members of a population having said disorder with the clinical
7 severity of said disorder,

8 thereby to determine the clinical severity of the disorder characterized by abnormal tissue aging
9 in said patient.

1 17. The method according to any one of claims 9-16, wherein the joint tissue sample
2 comprises a tissue selected from the group consisting of cartilage, ligament, meniscus, tendon,
3 synovium, synovial fluid, and intervertebral disc tissue.

1 18. The method according to any one of claims 9-16, wherein the joint tissue sample
2 comprises synovial fluid.

1 19. The method according to any one of claims 9, 11, 13, or 15, wherein the step of
2 determining an amount of OP-1 protein present in the joint tissue comprises performing an
3 enzyme-linked immunosorbent assay (ELISA).

1 20. The method according to any one of claims 9, 10, 13 or 14, wherein the age-related tissue
2 disorder is independent of chronological age.

1 21. The method according to any one of claims 9, 10, 13 or 14, wherein the age-related tissue
2 disorder is indicative of a disease selected from the group consisting of osteoarthritis and
3 osteoporosis.

- 1 22. The method according to any one of claims 11, 12, 15, or 16, wherein the disorder
2 characterized by abnormal tissue aging is a degenerative diseases.
- 1 23. The method according to any one of claims 9, 10, 11, or 12, wherein the predetermined
2 standard is age-correlated.
- 1 23. A method of determining the presence of an autoimmune disease in a patient, the method
2 comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample from the
4 patient; and
- 5 (b) comparing said amount of OP-1 protein with a predetermined standard;
6 wherein a difference in the amount of OP-1 protein present in said sample and the predetermined
7 standard is indicative of the presence of an autoimmune disease.
- 1 24. A method of determining the presence of an autoimmune disease in a patient, the method
2 comprising the steps of
- 3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample from the
4 patient; and
- 5 (b) comparing said amount of OP-1 mRNA with a predetermined standard;
6 wherein a difference in the amount of OP-1 mRNA present in said sample and the predetermined
7 standard is indicative of the presence of an autoimmune disease.
- 1 25. A method for determining the clinical severity of an autoimmune disease in a patient, the
2 method comprising the steps of
- 3 (a) determining an amount of OP-1 protein present in a joint tissue sample; and
- 4 (b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 protein present in joint tissue samples

6 obtained from members of a population having said autoimmune disease with the clinical
7 severity of said disease,

8 thereby to determine the clinical severity of the autoimmune disease in said patient.

1 26. A method for determining the clinical severity of an autoimmune disease in a patient, the
2 method comprising the steps of

3 (a) determining an amount of OP-1 mRNA present in a joint tissue sample; and

4 (b) applying to said amount a predetermined statistical relationship, said statistical
5 relationship correlating a range of amounts of OP-1 mRNA present in joint tissue
6 samples obtained from members of a population having said autoimmune disease with
7 the clinical severity of said disease,

8 thereby to determine the clinical severity of the autoimmune disease in said patient.

1 27. The method of any one of claims 23-26, wherein said autoimmune disease is associated
2 with a histomorphological change in a joint tissue.

2 28. The method of any one of claims 23-26, wherein the joint tissue sample comprises a
3 tissue selected from the group consisting of cartilage, ligament, meniscus, tendon, synovium,
3 synovial fluid, and intervertebral disc tissue.

1 29. The method of any one of claims 23-26, wherein the joint tissue sample comprises
2 synovial fluid.

1 30. The method of claim 23 or 25, wherein the step of determining an amount of OP-1
2 protein present in the joint tissue sample comprises performing an enzyme-linked
3 immunosorbent assay (ELISA).

1 31. The method of any one of claims 23-26, wherein the autoimmune disease is selected from
2 the group consisting of rheumatoid arthritis, lupus erythematosus and non-inflammatory
3 monoarthritis, and psoriasis.

1 32. The method of any one of claims 1, 2, 9, 10, 11, 12, 23 or 24, wherein the predetermined
2 standard comprises a range of values.

1 33. The method of claim 1, 2, 9, 10, 11, 12, 23 or 24, wherein the predetermined standard is
2 an age-adjusted standard.

1 34. A method of determining a predisposition for a disease which results in cartilage
2 degradation or degeneration in a patient, the method comprising the steps of

3 (a) determining an amount of OP-1 protein present in a joint tissue sample from the
4 patient; and

5 (b) comparing said amount of OP-1 protein with a predetermined standard;

6 wherein a difference in the amount of OP-1 protein present in said sample and the predetermined
7 standard is indicative of a predisposition for the inflammatory disease, disorder characterized by
8 abnormal tissue aging in a patient, autoimmune disease, joint degenerative disease, and/or joint
9 trauma-induced disease.

1 35. A method of determining the clinical status of a joint region of a patient, the method
2 comprising the steps of:

3 (a) determining an amount of OP-1 protein present in a tissue sample obtained from a
4 joint region of a patient;

5 (b) comparing said amount with a predetermined standard, thereby to determine a value
6 representative of the deviation of said amount with said standard,

7 wherein said value is indicative of the clinical status of said joint region.

1 36. A method according to claim 35, wherein said predetermined standard is correlated with
2 the age of said patient and is representative of an amount of OP-1 protein expected to be present
3 in a clinically-normal joint region.

1 37. A method according to claim 35, wherein said predetermined standard comprises a range
2 of values.

1 38. A method of monitoring regenerative or degenerative activity within a joint region of a
2 patient, the method comprising the steps of:

3 determining the relative amount of OP-1 protein present in at least one tissue sample
4 obtained from the joint region of said patient, wherein the at least one said tissue sample
5 corresponds to a point in time which is later than a first, earlier tissue sample for which OP-1
6 protein amounts are already determined,

7 wherein an increase in the amount of OP-1 protein present in said later tissue sample is
8 indicative of an onset of, or increase in, regenerative activity in said joint region, and whereas a
9 decrease in the amount of OP-1 protein present in said later tissue sample is indicative of a
10 cessation of, or decrease in, regenerative activity in said joint region.

1 39. A method of determining the clinical status of a joint region of a patient, the method
2 comprising the steps of:

3 (a) determining an amount of OP-1 protein present in a tissue sample obtained from a
4 joint region of a patient; and

5 (b) comparing said amount with a predetermined standard indicative of an amount of OP-
6 1 protein expected to be present in a clinically normal joint region,

7 wherein an amount determined in step (a) that is about equal to said standard is indicative
8 of a normal clinical status of said joint region of said patient, and an amount that is not about
9 equal to said standard is indicative of an abnormal clinical status of said joint region of said
10 patient.

1 40. A method for determining the effective dose of an anti-inflammatory agent in a subject,
2 the method comprising the steps of:

3 (a) obtaining a tissue, body fluid or cell sample from a subject to whom a dose of an anti-
4 inflammatory agent is earlier administered ;

5 (b) determining OP-1 protein concentration or OP-1 mRNA concentration in said sample;

6 (c) determining in said same sample the concentration of protein or mRNA encoded by a

7 second gene whose expression is not altered by inflammation; and

8 (d) comparing the OP-1 protein or mRNA concentration to the protein or mRNA

9 concentration of the second gene, wherein the difference between the OP-1 protein or mRNA

10 concentration and the second gene protein or mRNA concentration is indicative of the

11 effectiveness of the anti-inflammatory agent dose in the patient.

1 41. A method for determining the ability of a patient to respond to an anti-inflammatory
2 agent, the method comprising the steps of:

3 (a) obtaining a tissue, body fluid or cell sample from a subject to whom a dose of an anti-
4 inflammatory agent was earlier administered;

5 (b) determining OP-1 protein concentration or OP-1 mRNA concentration in said sample;

6 (c) determining in said same sample the concentration of protein or mRNA encoded by a

7 second gene whose expression is not altered by inflammation; and

8 (d) comparing the OP-1 protein or mRNA concentration to the protein or mRNA

9 concentration of the second gene to create a ratio, wherein the subject is responsive to an anti-
10 inflammatory agent if the ratio is higher than a predetermined control ratio for untreated or
11 nonresponsive subjects, or similar to prior ratios for the subject when the subject was previously
12 determined to be responsive.

1 42. The method of any one of claims 1-4, wherein the inflammatory disease is rheumatoid
2 arthritis.

1 43. The method of any one of claims 9, 10, 13 or 14, wherein the age-related tissue disorder
2 is osteoarthritis.

1 44. The method of any one of claims 23-26, wherein the autoimmune disease is rheumatoid
2 arthritis.

- 1 45. A method of determining joint tissue deterioration, including deterioration associated
2 with disease or age, the method comprising the steps of:
3 (a) determining in a joint tissue sample an amount of bone morphogenic protein related to
4 OP-1 or an amount of mRNA encoding a protein related to OP-1; and
5 (b) comparing said amount of protein or mRNA with a predetermined standard;
6 wherein a difference in the amount of protein or mRNA in said sample and the predetermined
7 standard is indicative of joint tissue deterioration.
- 1 46. A method of determining joint tissue aging, including premature aging associated with
2 disease, the method comprising the steps of:
3 (a) determining in a joint tissue sample an amount of bone morphogenic protein related to
4 OP-1 or an amount of mRNA encoding a protein related to OP-1; and
5 (b) comparing said amount of protein or mRNA with a predetermined standard;
6 wherein a difference in the amount of protein or mRNA in said sample and the predetermined
7 standard is indicative of joint tissue aging.